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[General] [Name and origin] [References] [Comments] [Cross-references] [Keywords] [Features] [Sequence] [Tools]

General information about the entry	
Entry name	**BXB_CLOBO**
Primary accession number	**P10844**
Secondary accession number	P10843
Entered in SWISS-PROT in	Release 11, July 1989
Sequence was last modified in	Release 26, July 1993
Annotations were last modified in	Release 41, June 2002
Name and origin of the protein	
Protein name	**Botulinum neurotoxin type B [Precursor]**
Synonyms	**EC 3.4.24.69** **BoNT/B** **Bontoxilysin B**
Gene name	**BOTB**
From	Clostridium botulinum [TaxID: 1491]
Taxonomy	Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae; Clostridium.

References

[1]	SEQUENCE FROM NUCLEIC ACID. MEDLINE=92384550; PubMed=1514783; [NCBI, ExPASy, EBI, Israel, Japan] Whelan S.M., Elmore M.J., Bodsworth N.J., Brehm J.K., Atkinson T., Minton N.P.; "Molecular cloning of the Clostridium botulinum structural gene encoding the type B neurotoxin and determination of its entire nucleotide sequence."; Appl. Environ. Microbiol. 58:2345-2354(1992).
[2]	SEQUENCE OF 35-245 FROM NUCLEIC ACID. **STRAIN**=NCTC 7273; Szabo E.A., Pemberton J.M., Desmarchelier P.M.; Submitted (APR-1992) to the EMBL/GenBank/DDBJ databases.
[3]	SEQUENCE OF 633-993 FROM NUCLEIC ACID. **STRAIN**=NCTC 7273; MEDLINE=94013372; PubMed=8408542; [NCBI, ExPASy, EBI, Israel, Japan] Campbell K., East A.K., Collins M.D.; "Gene probes for identification of the botulinal neurotoxin gene and specific identification of neurotoxin types B, E, and F."; J. Clin. Microbiol. 31:2255-2262(1993).
[4]	SEQUENCE OF 1-44 AND 441-466. **STRAIN**=657; MEDLINE=89000987; PubMed=3139097; [NCBI, ExPASy, EBI, Israel, Japan] Dasgupta B.R., Datta A.; "Botulinum neurotoxin type B (strain 657): partial sequence and similarity with tetanus toxin."; Biochimie 70:811-817(1988).
[5]	SEQUENCE OF 1-16 AND 441-458. **STRAIN**=OKRA; MEDLINE=85197963; PubMed=3888113; [NCBI, ExPASy, EBI, Israel, Japan]

	Schmidt J.J., Sathyamoorthy V., Dasgupta B.R.; "Partial amino acid sequences of botulinum neurotoxins types B and E."; Arch. Biochem. Biophys. 238:544-548(1985).
[6]	IDENTIFICATION AS ZINC-PROTEASE. MEDLINE=93054694; PubMed=1429690; [NCBI, ExPASy, EBI, Israel, Japan] Schiavo G., Rossetto O., Santucci A., Dasgupta B.R., Montecucco C.; "Botulinum neurotoxins are zinc proteins."; J. Biol. Chem. 267:23479-23483(1992).
[7]	IDENTIFICATION OF SUBSTRATE. MEDLINE=93063293; PubMed=1331807; [NCBI, ExPASy, EBI, Israel, Japan] Schiavo G., Benfenati F., Poulain B., Rossetto O., de Laureto P.P., Dasgupta B.R., Montecucco C.; "Tetanus and botulinum-B neurotoxins block neurotransmitter release by proteolytic cleavage of synaptobrevin."; Nature 359:832-835(1992).

Comments

FUNCTION: BOTULINUS TOXIN ACTS BY INHIBITING NEUROTRANSMITTER RELEASE. IT BINDS TO PERIPHERAL NEURONAL SYNAPSES, IS INTERNALIZED AND MOVES BY RETROGRADE TRANSPORT UP THE AXON INTO THE SPINAL CORD WHERE IT CAN MOVE BETWEEN POSTSYNAPTIC AND PRESYNAPTIC NEURONS. IT INHIBITS NEUROTRANSMITTER RELEASE BY ACTING AS A ZINC ENDOPEPTIDASE THAT CLEAVES THE 76-GLN-|-PHE-77 BOND OF SYNAPTOBREVIN-2.

CATALYTIC ACTIVITY: Limited hydrolysis of proteins of the neuroexocytosis apparatus, synaptobrevins, SNAP25 or syntaxin. No detected action on small molecule substrates.

COFACTOR: Binds 1 zinc ion per subunit *(By similarity)*.

SUBUNIT: DISULFIDE-LINKED HETERODIMER OF A LIGHT CHAIN (L) AND A HEAVY CHAIN (H). THE LIGHT CHAIN HAS THE PHARMACOLOGICAL ACTIVITY, WHILE THE N-AND C-TERMINAL OF THE HEAVY CHAIN MEDIATE CHANNEL FORMATION AND TOXIN BINDING, RESPECTIVELY.

SUBCELLULAR LOCATION: Secreted.
MISCELLANEOUS: THERE ARE SEVEN ANTIGENICALLY DISTINCT FORMS OF BOTULINUM NEUROTOXIN: TYPES A, B, C1, D, E, F, AND G.
SIMILARITY: BELONGS TO PEPTIDASE FAMILY M27.

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Cross-references

EMBL	M81186; AAA23211.1; -. Z11934; CAA77991.1; -. X70817; CAA50148.1; -.	[EMBL / GenBank / DDBJ] [CoDingSequence] [EMBL / GenBank / DDBJ] [CoDingSequence] [EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	S07128; S07128. S07155; S07155. S08562; S08562. S08573; S08573. S08574; S08574. A48940; A48940.	
HSSP	P10845; 3BTA. [HSSP ENTRY / PDB]	
MEROPS	M27.002; -.	
InterPro	IPR000395; Bontoxilysin. IPR000130; Zn_MTpeptdse. Graphical view of domain structure.	
Pfam	PF01742; Peptidase_M27; 1.	
PRINTS	PR00760; BONTOXILYSIN.	
ProDom	PD001963; Bontoxilysin; 1. [Domain structure / List of seq. sharing at least 1 domain].	
PROSITE	PS00142; ZINC_PROTEASE; 1.	
BLOCKS	P10844	

BLOCKS	P10844.
ProtoNet	P10844.
ProtoMap	P10844.
PRESAGE	P10844.
DIP	P10844.
ModBase	P10844.
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Keywords

Neurotoxin; Transmembrane; Hydrolase; Metalloprotease; Zinc.

Features

Key	From	To	Length	Description
INIT_MET	0	0		
CHAIN	1	440	440	BOTULINUM NEUROTOXIN B, LIGHT-CHAIN.
CHAIN	441	1290	850	BOTULINUM NEUROTOXIN B, HEAVY-CHAIN.
METAL	229	229		ZINC (CATALYTIC) (*BY SIMILARITY*).
ACT_SITE	230	230		*BY SIMILARITY*.
METAL	233	233		ZINC (CATALYTIC) (*BY SIMILARITY*).
DISULFID	436	445		INTERCHAIN (*PROBABLE*).
CONFLICT	29	29		T -> M (IN REF. 4).
CONFLICT	217	217		R -> G (IN REF. 2).
CONFLICT	224	224		A -> S (IN REF. 2).
CONFLICT	463	463		S -> R (IN REF. 4).

Feature aligner

Feature table viewer

Sequence information

Length: **1290 AA** [This is the length of the unprocessed precursor]	Molecular weight: **150670 Da** [This is the MW of the unprocessed precursor]	CRC64: **D21746E2C024DF43** [This is a checksum on the sequence]

```
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          |          |          |          |          |          |
PVTINNFNYN DPIDNNNIIM MEPPFARGTG RYYKAFKITD RIWIIPERYT FGYKPEDFNK

         70         80         90        100        110        120
          |          |          |          |          |          |
SSGIFNRDVC EYYDPDYLNT NDKKNIFLQT MIKLFNRIKS KPLGEKLLEM IINGIPYLGD

        130        140        150        160        170        180
```

```
RRVPLEEFNT NIASVTVNKL ISNPGEVERK KGIFANLIIF GPGPVLNENE TIDIGIQNHF

       190        200        210        220        230        240
ASREGFGGIM QMKFCPEYVS VFNNVQENKG ASIFNRRGYF SDPALILMHE LIHVLHGLYG

       250        260        270        280        290        300
IKVDDLPIVP NEKKFFMQST DAIQAEELYT FGGQDPSIIT PSTDKSIYDK VLQNFRGIVD

       310        320        330        340        350        360
RLNKVLVCIS DPNININIYK NKFKDKYKFV EDSEGKYSID VESFDKLYKS LMFGFTETNI

       370        380        390        400        410        420
AENYKIKTRA SYFSDSLPPV KIKNLLDNEI YTIEEGFNIS DKDMEKEYRG QNKAINKQAY

       430        440        450        460        470        480
EEISKEHLAV YKIQMCKSVK APGICIDVDN EDLFFIADKN SFSDDLSKNE RIEYNTQSNY

       490        500        510        520        530        540
IENDFPINEL ILDTDLISKI ELPSENTESL TDFNVDVPVY EKQPAIKKIF TDENTIFQYL

       550        560        570        580        590        600
YSQTFPLDIR DISLTSSFDD ALLFSNKVYS FFSMDYIKTA NKVVEAGLFA GWVKQIVNDF

       610        620        630        640        650        660
VIEANKSNTM DKIADISLIV PYIGLALNVG NETAKGNFEN AFEIAGASIL LEFIPELLIP

       670        680        690        700        710        720
VVGAFLLESY IDNKNKIIKT IDNALTKRNE KWSDMYGLIV AQWLSTVNTQ FYTIKEGMYK

       730        740        750        760        770        780
ALNYQAQALE EIIKYRYNIY SEKEKSNINI DFNDINSKLN EGINQAIDNI NNFINGCSVS

       790        800        810        820        830        840
YLMKKMIPLA VEKLLDFDNT LKKNLLNYID ENKLYLIGSA EYEKSKVNKY LKTIMPFDLS

       850        860        870        880        890        900
IYTNDTILIE MFNKYNSEIL NNIILNLRYK DNNLIDLSGY GAKVEVYDGV ELNDKNQFKL

       910        920        930        940        950        960
TSSANSKIRV TQNQNIIFNS VFLDFSVSFW IRIPKYKNDG IQNYIHNEYT IINCMKNNSG

       970        980        990       1000       1010       1020
WKISIRGNRI IWTLIDINGK TKSVFFEYNI REDISEYINR WFFVTITNNL NNAKIYINGK

      1030       1040       1050       1060       1070       1080
LESNTDIKDI REVIANGEII FKLDGDIDRT QFIWMKYFSI FNTELSQSNI EERYKIQSYS

      1090       1100       1110       1120       1130       1140
```

```
EYLKDFWGNP LMYNKEYYMF NAGNKNSYIK LKKDSPVGEI LTRSKYNQNS KYINYRDLYI

      1150       1160       1170       1180       1190       1200
         |          |          |          |          |          |
GEKFIIRRKS NSQSINDDIV RKEDYIYLDF FNLNQEWRVY TYKYFKKEEE KLFLAPISDS

      1210       1220       1230       1240       1250       1260
         |          |          |          |          |          |
DEFYNTIQIK EYDEQPTYSC QLLFKKDEES TDEIGLIGIH RFYESGIVFE EYKDYFCISK

      1270       1280       1290
         |          |          |
WYLKEVKRKP YNLKLGCNWQ FIPKDEGWTE
```

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Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)

Feature table viewer (Java)

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Search notes 10/02

NiceProt View of TrEMBL: Q9R540

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[General] [Name and origin] [References] [Comments] [Cross-references] [Keywords] [Features] [Sequence] [Tools]

General information about the entry

Entry name	**Q9R540**
Primary accession number	**Q9R540**
Secondary accession numbers	None
Entered in TrEMBL in	Release 13, May 2000
Sequence was last modified in	Release 13, May 2000
Annotations were last modified in	Release 15, October 2000

Name and origin of the protein

Protein name	**Neurotoxin heavy chain 18 kDa fragment [Fragment]**
Synonyms	None
Gene name	None
From	Clostridium botulinum [TaxID: 1491]
Taxonomy	Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae; Clostridium.

References

[1] SEQUENCE.
MEDLINE=94000342; PubMed=8397793; [NCBI, ExPASy, EBI, Israel, Japan]
Gimenez J.A., DasGupta B.R.;
"Botulinum type A neurotoxin digested with pepsin yields 132, 97, 72, 45, 42, and 18 kD fragments.";
J. Protein Chem. 12:351-363(1993).

Comments

None

Cross-references

HSSP	P10845; 3BTA. [HSSP ENTRY / PDB]
ProDom	[Domain structure / List of seq. sharing at least 1 domain].
ProtoMap	Q9R540.
PRESAGE	Q9R540.
ModBase	Q9R540.
SWISS-2DPAGE	GET REGION ON 2D PAGE.

Keywords

None

Features

None

Sequence information

Length: **72 AA**	Molecular weight: **8165 Da**	CRC64: **B7A959576A615E18** [This is a checksum on the sequence]

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        10         20         30         40         50         60
         |          |          |          |          |          |
IYLNSSLYRG TKFIIKKYAS GNKDNIVRNN DRVYINVVVK NKEYRLATNA SQAGVEKILS

        70
         |
ALEIPDVGNL YQ
```

Q9R540 in FASTA format

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Direct BLAST submission at NCBI (Bethesda, USA)

ScanProsite, MotifScan

Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)

Feature table viewer (Java)

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Fr m: Portner, Ginny
Sent: Tuesday, October 29, 2002 4:40 PM
To: STIC-ILL
Subject: 09/910,186 neurotoxin

Curr Microbiol 1994 Feb;28(2):101-10

Nucleotide sequence of the gene coding for non-proteolytic Clostridium botulinum type B neurotoxin: comparison with other clostridial neurotoxins.

Hutson RA, Collins MD, East AK, Thompson DE.

Department of Microbiology, AFRC Institute of Food Research, Reading Laboratory, UK.

Ginny Portner
CM1, Art Unit 1645
Room 7e13
Mail box 7e12
(703) 308-7543

Mic
QR1.A6

STIC-ILL

From: Portner, Ginny
Sent: Tuesday, October 29, 2002 4:46 PM
T : STIC-ILL
Subject: 09/910,186 neurotoxin

Appl Environ Microbiol 1993 Sep;59(9):3011-20

Detection of the genes encoding botulinum neurotoxin types A to E by the polymerase chain reaction.

Szabo EA, Pemberton JM, Desmarchelier PM.

Department of Microbiology, University of Queensland, Australia.

Ginny Portner
CM1, Art Unit 1645
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(703) 308-7543

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STIC-ILL

Fr m: Portner, Ginny
Sent: Tuesday, October 29, 2002 4:40 PM
To: STIC-ILL
Subject: 09/910,186 neurotoxin

Imp rtance: High

J Clin Microbiol 1993 Sep;31(9):2255-62

Gene probes for identification of the botulinal neurotoxin gene and specific identification of neurotoxin types B, E, and F.

Campbell KD, Collins MD, East AK.

Reading Laboratory, Institute of Food Research, Agriculture and Food Research Council, United Kingdom.

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(703) 308-7543

Appl. Environ. Microbiol., Aug 1992, 2345-2354, Vol 58, No. 8

Molecular cloning of the Clostridium botulinum structural gene encoding the type B neurotoxin and determination of its entire nucleotide sequence

SM Whelan, MJ Elmore, NJ Bodsworth, JK Brehm, T Atkinson and NP Minton

Division of Biotechnology, PHLS Centre for Applied Microbiology and Research, Salisbury, Wiltshire, United Kingdom.

DNA fragments derived from the Clostridium botulinum type A neurotoxin (BoNT/A) gene (botA) were used in DNA-DNA hybridization reactions to derive a restriction map of the region of the C. botulinum type B strain Danish chromosome encoding botB. As the one probe encoded part of the BoNT/A heavy (H) chain and the other encoded part of the light (L) chain, the position and orientation of botB relative to this map were established. The temperature at which hybridization occurred indicated that a higher degree of DNA homology occurred between the two genes in the H-chain-encoding region. By using the derived restriction map data, a 2.1-kb BglII-XbaI fragment encoding the entire BoNT/B L chain and 108 amino acids of the H

chain was cloned and characterized by nucleotide sequencing. A contiguous 1.8-kb XbaI fragment encoding a further 623 amino acids of the H chain was also cloned. The 3' end of the gene was obtained by cloning a 1.6-kb fragment amplified from genomic DNA by inverse polymerase chain reaction. Translation of the nucleotide sequence derived from all three clones demonstrated that BoNT/B was composed of 1,291 amino acids. Comparative alignment of its sequence with all currently characterized BoNTs (A, C, D, and E) and tetanus toxin (TeTx) showed that a wide variation in percent homology occurred dependent on which component of the dichain was compared. Thus, the L chain of BoNT/B exhibits the greatest degree of homology (50% identity) with the TeTx L chain, whereas its H chain is most homologous (48% identity) with the BoNT/A H chain. Overall, the six neurotoxins were shown to be composed of highly conserved amino acid domains interceded with amino acid tracts exhibiting little overall similarity. In total, 68 amino acids of an average of 442 are absolutely conserved between L chains and 110 of 845 amino acids are conserved between H chains. Conservation of Trp residues (one in the L chain and nine in the H chain) was particularly striking. The most divergent region corresponds to the extreme carboxy terminus of each toxin, which may reflect differences in specificity of binding to neurone acceptor sites.

This article has been cited by other articles:

Lindstrom, M., Keto, R., Markkula, A., Nevas, M., Hielm, S., Korkeala, H. (2001). Multiplex PCR Assay for Detection and Identification of Clostridium botulinum Types A, B, E, and F in Food and Fecal Material. *Appl. Environ. Microbiol.* 67: 5694-5699 [Abstract] [Full Text]

Kimura, B., Kawasaki, S., Nakano, H., Fujii, T. (2001). Rapid, Quantitative PCR Monitoring of Growth of Clostridium botulinum Type E in Modified-Atmosphere-Packaged Fish. *Appl. Environ. Microbiol.* 67: 206-216 [Abstract] [Full Text]

Hutson, R. A., Zhou, Y., Collins, M. D., Johnson, E. A., Hatheway, C. L., Sugiyama, H. (1996). Genetic Characterization of Clostridium botulinum

Type A Containing Silent Type B Neurotoxin Gene Sequences. *J. Biol. Chem.* 271: 10786-10792 [Abstract] [Full Text]
Shapiro, R. E., Specht, C. D., Collins, B. E., Woods, A. S., Cotter, R. J., Schnaar, R. L. (1997). Identification of a Ganglioside Recognition Domain of Tetanus Toxin Using a Novel Ganglioside Photoaffinity Ligand. *J. Biol. Chem.* 272: 30380-30386 [Abstract] [Full Text]

1: J Clin Microbiol 1994 Aug;32(8):1911-7

Related Ar

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Detection of type A, B, and E botulism neurotoxin genes in Clostridium botulinum and other Clostridium species by PCR: evidence o unexpressed type B toxin genes in type A toxigenic organisms.

Franciosa G, Ferreira JL, Hatheway CL.

PubMed Services

Istituto Superiore di Sanita, Laboratorio Alimenti, Ro Italy.

We studied the effectiveness of the PCR in detecting type A, B, and E botulism neurotoxin genes in 209 stra Clostridium botulinum and 29 strains of other Clostrid spp. All 79 strains that produced type A toxin, 77 strc that produced type B toxin, and 51 organisms that pro type E toxin (46 C. botulinum and 5 C. butyricum) were positive in reactions with primers targeting sequences specific for their respective toxin genes. The PCR for A toxin was positive for one type B toxin-producing st that produced a small amount of type A toxin in additi a large amount of type B toxin. Surprisingly, the type

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toxin gene was detected in addition to the type A toxi
gene in 43 type A toxin-producing strains, only 1 of wh
could be shown by bioassay to produce biologically act
type B toxin in culture. The type B gene was also dete
in two strains of C. subterminale, which were determir
be nontoxigenic by bioassay. While the PCR was sensit
and specific in detecting the neurotoxin genes, the
discovery of unexpressed toxin genes indicates that P
results may not be adequate for establishing type B
neurotoxigenicity.

PMID: 7989542 [PubMed - indexed for MEDLINE]

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1: J Appl Bacteriol 1994 Jun;76(6):539-45

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Polymerase chain reaction for detection of Clostridium botulinum types A, B and E in foc soil and infant faeces.

Szabo EA, Pemberton JM, Gibson AM, Eyles MJ, Desmarchelier PM.

PubMed Services

Department of Microbiology, University of Queenslan Australia.

The application of the polymerase chain reaction (PCR detection of Clostridium botulinum types A, B and E in foods, environmental and clinical samples was evaluate compared to the mouse bioassay. Samples inoculated v 10, 100 and 1000 spores of Cl. botulinum types A and E included pasteurized milk, UHT milk, infant formula, ir faeces, meat juice, canned tuna, mushrooms, blood sau and soil. Clostridium botulinum type E spores were inoculated into fish eggs, canned tuna, picked herring, fish and soil at similar levels. Spores were added to 2. each sample with the exception of soil which was inoc in 10 g samples. The presence of Cl. botulinum in sampl

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enrichments was determined by both PCR and the bioa
An overall correlation of 95.6% was observed betweer
results and the mouse bioassay. Of the total of 114 sa
tested there was disparity between the mouse bioassa
the PCR in three samples of soil inoculated with 100 ty
or E spores and 10 type B spores per 10 g, respectivel
two samples of infant faeces inoculated with 10 type A
spores per 2.5 g. All of these samples gave negative ar
results and positive PCR results.

PMID: 8027003 [PubMed - indexed for MEDLINE]

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1: Eur J Biochem 1993 Nov 1;217(3):965-71

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Proteolytic cleavage of synthetic fragments c vesicle-associated membrane protein, isoforn by botulinum type B neurotoxin.

Shone CC, Quinn CP, Wait R, Hallis B, Fooks SG, Hambleton P.

PubMed Services

Centre for Applied Microbiology and Research, Porton Down, England.

Recent data suggest that botulinum type-B neurotoxin protease which acts on vesicle-associated membrane protein, isoform 2 (VAMP-2). In this report, botulinum type-B neurotoxin is shown to cleave a synthetic fragr (HV62) of VAMP-2, corresponding to the bulk of the hydrophilic domain (amino acids 33-94). The neurotoxi at a single site between Gln76 and Phe77. Little or no proteolytic activity by botulinum type-B neurotoxin wc observed with peptides containing 7, 10 or 20 amino ac spanning the site of cleavage. The proteolytic action o neurotoxin was strongly inhibited by EDTA and o-phenanthroline whereas captopril and phosphoramid

Related Resources

were ineffective. A series of model peptide substrate were synthesised in order to define the smallest VAM fragment to be cleaved by botulinum type-B neurotoxi Data obtained from these substrates suggest that th neurotoxin belongs to a novel class of zinc-endoprotea more than 12 amino acid residues are required on both NH2- and COOH-terminal side of the cleavage site fo optimal proteolytic activity. The results demonstrate no other components of cellular vesicles are required the specific action of the neurotoxin on VAMP-2. The further show that the highly specific action of the neurotoxin is not dictated solely by the properties of amino acid residues at the cleavage site but is also dependent on amino acid sequences distal to its site of action.

PMID: 8223654 [PubMed - indexed for MEDLINE]

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☐1: Appl Environ Microbiol 1993 Sep;59(9):3011-20 Related Art

Detection of the genes encoding botulinum neurotoxin types A to E by the polymerase ch reaction.

Szabo EA, Pemberton JM, Desmarchelier PM.

Department of Microbiology, University of Queensland, Australia.

The polymerase chain reaction (PCR) was used as the ba for the development of highly sensitive and specific diagnostic tests for organisms harboring botulinum neurotoxin type A through E genes. Synthetic DNA prin were selected from nucleic acid sequence data for Clostridium botulinum neurotoxins. Individual componen the PCR for each serotype (serotypes A through E) wer adjusted for optimal amplification of the target fragme Each PCR assay was tested with organisms expressing e of the botulinum neurotoxin types (types A through G), Clostridium tetani, genetically related nontoxigenic organisms, and unrelated strains. Each assay was specifi the intended target. The PCR reliably identified multipl strains having the same neurotoxin type. The sensitivity

1: Arch Biochem Biophys 1985 May 1;238(2):544-8

Partial amino acid sequences of botulinum neurotoxins types B and E.

Schmidt JJ, Sathyamoorthy V, DasGupta BR.

Clostridium botulinum type E neurotoxin, a single-chain protein of Mr 147,000, was purified and subjected to a acid sequencing. The same was done for single-chain botulinum type B neurotoxin (Mr 152,000), and for the l and light chains (Mr 104,000 and 51,000 respectively) derived from type B by limited trypsin digestion. Twelv eighteen residues were identified and the following conclusions were drawn: The light chain of the nicked (dichain) type B is derived from the N-terminal one-thi the single-chain (unnicked) parent neurotoxin; sequence homologies are present between single-chain types B an and the light chain of the nicked type A [J. J. Schmidt, Sathyamoorthy, and B. R. DasGupta (1984) Biochem. Bio Res. Commun. 119, 900-904]; the N-terminal regions of heavy chains of types A and B have some structural similarity; and activation of type B neurotoxin cannot in removal of amino acids or peptides from the N terminus

PMID: 3888113 [PubMed - indexed for MEDLINE]

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1: Appl Environ Microbiol 1992 Jan;58(1):418-20

Related Art

Specific detection of Clostridium botulinum ty by using the polymerase chain reaction.

Szabo EA, Pemberton JM, Desmarchelier PM.

Department of Microbiology, University of Queensland, Australia.

The polymerase chain reaction (PCR) and a radiolabeled oligonucleotide probe were used to specifically detect proteolytic and nonproteolytic Clostridium botulinum ty Two synthetic primers deduced from the amino acid sequence data of type B neurotoxin were used to amplif 1.5-kbp fragment corresponding to the light chain of th toxin. Although, nonspecific priming was observed when PCR protocol was tested with other clostridial species, the PCR product from C. botulinum type B isolates reac with the radiolabeled internal probe. As little as 100 fg DNA (approximately 35 clostridial cells) could be detec after only 25 amplification cycles.

PMID: 1539990 [PubMed - indexed for MEDLINE]

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1: Adv Exp Med Biol 1996;389:251-60 Related Articles, L

Tetanus and botulism neurotoxins: a novel grou of zinc-endopeptidases.

Tonello F, Morante S, Rossetto O, Schiavo G, Montecucco C.

Centro CNR Biomembrane and Dipartimento di Scienze Biomediche, Universita di Padova, Italy.

Tetanus and botulinum neurotoxins are produced by bac of the genus Clostridium and cause the paralytic syndro of tetanus and botulism with a persistent inhibition of neurotransmitter release at central and peripheral syna respectively. These neurotoxins consist of two disulfide-linked polypeptides: H (100 kDa) is responsible neurospecific binding and cell penetration of L(50 kDa), zinc-endopeptidase specific for three protein subunits the neuroexocytosis apparatus. Tetanus neurotoxin and botulinum neurotoxins serotypes B, D, F, and G cleave a single sites, which differ for each neurotoxin. VAMP/synaptobrevin, a membrane protein of the synapt vesicles. Botulinum A and E neurotoxins cleave SNAP-25 protein of the presynaptic membrane, at two different carboxyl-terminal peptide bonds. Serotype C cleaves

specifically syntaxin, another protein of the nerve plasmalemma. The target specificity of these metallo-proteinases relies on a double recognition of th substrates based on interactions with the cleavage site with a non contiguous segment that contains a structur motif common to VAMP, SNAP-25 and syntaxin.

Publication Types:

- Review
- Review, Tutorial

PMID: 8861019 [PubMed - indexed for MEDLINE]

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J Clin Microbiol 1994 Aug;32(8):1986-91

Related Articles, Links

Application of PCR to a clinical and environmental investigation of a case of equine botulism.

Szabo EA, Pemberton JM, Gibson AM, Thomas RJ, Pascoe RR, Desmarchelier PM.

Department of Microbiology, University of Queensland, St. Lucia, Australia.

PCR for the detection of botulinum neurotoxin gene types A to E was used in the investigation of a case of equine botulism. Samples from a foal diagnosed with toxicoinfectious botulism in 1985 were reanalyzed by PCR and the mouse bioassay in conjunction with an environmental survey. Neurotoxin B was detected by mouse bioassay in culture enrichments of serum, spleen, feces, and intestinal contents. PCR results compared well with mouse bioassay results, detecting type B neurotoxin genes in these samples and also in a liver sample. Other neurotoxin types were not detected by either test. Clostridium botulinum type B was shown to be prevalent in soils collected from the area in which the foal was raised. Four methods were used to test for the presence of botulinum neurotoxin-producing organisms in 66 soil samples taken within a 5-km radius: PCR and agarose gel electrophoresis (types A to E), PCR and an enzyme-linked assay (type B), hybridization of crude alkaline cell lysates with a type B-specific probe, and the mouse bioassay (all types). Fewer soil samples were positive for C. botulinum type B by the mouse bioassay (15%) than by any of the DNA-based detection systems. Hybridization of a type B-specific probe to DNA dot blots (26% of the samples were positive) and PCR-enzyme-linked assay (77% of the samples were positive) were used for the rapid analysis of large numbers of samples, with sensitivity limits of 3 x 10(6) and 3,000 cells, respectively. Conventional detection of PCR products by gel electrophoresis was the most sensitive method (300-cell limit), and in the present environmental survey, neurotoxin B genes only were detected in 94% of the samples.

PMID: 7989554 [PubMed - indexed for MEDLINE]

Curr Microbiol 1994 Feb;28(2):101-10

Nucleotide sequence of the gene coding for non-proteolytic Clostridium botulinum type B neurotoxin: comparison with other clostridial neurotoxins.

Hutson RA, Collins MD, East AK, Thompson DE.

Department of Microbiology, AFRC Institute of Food Research, Reading Laboratory, UK.

The neurotoxin gene of non-proteolytic Clostridium botulinum type B (strain Eklund 17B) was cloned as a series of overlapping polymerase chain reaction (PCR) fragments generated with primers designed to conserved regions of published botulinal toxin (BoNT) sequences. The 3' end of the gene was obtained by using primers designed to the determined sequence of non-proteolytic BoNT/B and a published downstream region of BoNT/B gene from a proteolytic strain. Translation of the nucleotide sequence derived from cloned PCR fragments demonstrated the toxin gene encodes a protein of 1291 amino acid residues. Comparative alignment of the derived BoNT/B sequence with those of other published botulinal neurotoxins revealed highest sequence relatedness with BoNT/B of proteolytic C. botulinum. The sequence identity between non-proteolytic and proteolytic BoNT/B was 97.7% for the light chain (corresponding to 10 amino acid changes) and 90.2% for the heavy chain (corresponding to 81 amino acid changes), with most differences occurring at the C-terminal end. A genealogical tree constructed from all known botulinal neurotoxin sequences revealed marked topological differences with a phylogenetic tree of C. botulinum types based upon small-subunit (16S) ribosomal RNA sequences.

Biochim Biophys Acta 1993 Dec 14;1216(3):487-91

Nucleotide sequence of the gene coding for Clostridium botulinum (Clostridium argentinense) type G neurotoxin: genealogical comparison with other clostridial neurotoxins.

Campbell K, Collins MD, East AK.

Department of Microbiology, Institute of Food Research, Reading Laboratory, Earley Gate, UK.

The neurotoxin gene from Clostridium botulinum type G was cloned as a series of overlapping DNA fragments generated using polymerase chain reaction (PCR) technology and primers designed to conserved regions of published botulinal toxin (BoNT) sequences. The 5'-end of the gene was obtained using a primer based on a conserved region of the nontoxic-nonhaemagglutinin gene lying upstream of the toxin gene. Translation of the nucleotide sequence derived from the cloned PCR fragments demonstrated that the gene encodes a protein of 1297 amino acid residues (rmm 149, 147). Comparative alignment of the determined BoNT/G sequence with those of other clostridial neurotoxins revealed highest sequence relatedness (approx. 58% amino acid identity) with BoNT/B of proteolytic and non-proteolytic C. botulinum. Tetanus toxin (TeTx) and other BoNT types revealed lower levels of relatedness with BoNT/G (approximate range 35-42% amino acid identity).

PMID: 8268233 [PubMed - indexed for MEDLINE]

Microbiol Rev 1993 Dec;57(4):823-37

Bacterial extracellular zinc-containing metalloproteases.

Hase CC, Finkelstein RA.

Department of Molecular Microbiology and Immunology, School of Medicine, University of Missouri, Columbia 65212.

Extracellular zinc-containing metalloproteases are widely distributed in the bacterial world. The most extensively studied are those which are associated with pathogenic bacteria or bacteria which have industrial significance. They are found practically wherever they are sought in both gram-negative and gram-positive microorganisms, be they aerobic or anaerobic. This ubiquity in itself implies that these enzymes serve important functions for the organisms which produce them. Because of the importance of zinc to enzymatic activity, it is not surprising that there is a pervasive amino acid sequence homology in the primary structure of this family of enzymes regardless of their source. The evidence suggests that both convergent and divergent evolutionary forces are at work. Within the large family of bacterial zinc-containing metalloendopeptidases, smaller family units are observed, such as thermolysin-like, elastase-like, and Serratia protease-like metalloproteases from various bacterial species. While this review was in the process of construction, a new function for zinc-containing metalloproteases was discovered: the neurotoxins of Clostridium tetani and Clostridium botulinum type B have been shown to be zinc metalloproteases with specificity for synaptobrevin, an integral membrane protein of small synaptic vesicles which is involved in neurotransmission. Additional understanding of the mode of action of proteases which contribute to pathogenicity could lead to the development of inhibitors, such as chelators, surrogate substrates, or antibodies, which could prevent or interrupt the disease process. Further studies of this broad family of metalloproteases will provide important additional insights into the pathogenesis and structure-function relationships of enzymes and will lead to the development of products, including "designer proteins," which might be industrially and/or therapeutically useful.

Publication Types:
Review
Review, Academic

PMID: 8302217 [PubMed - indexed for MEDLINE]

Antonie Van Leeuwenhoek 1993-94;64(3-4):273-83

Related Articles, Links

Genetic interrelationships of proteolytic Clostridium botulinum types A, B, and F and other members of the Clostridium botulinum complex as revealed by small-subunit rRNA gene sequences.

Hutson RA, Thompson DE, Lawson PA, Schocken-Itturino RP, Bottger EC, Collins MD.

Department of Microbiology, AFRC Institute of Food Research, Reading Laboratory, UK.

The phylogenetic interrelationships of members of the Clostridium botulinum complex of species was investigated by direct sequencing of their 16S rRNA genes. Comparative analysis of the 16S rRNA sequences demonstrated the presence of four phylogenetically distinct lineages corresponding to: i) proteolytic C. botulinum types A, B, and F, and C. sporogenes, ii) saccharolytic types B, E and F, iii) types C and D and C. novyi type A, and iv) type G and C. subterminale. The phylogenetic groupings obtained from the 16S rRNA were in complete agreement with the four divisions recognised within the the 'species complex' on the basis of phenotypic criteria.

PMID: 8085790 [PubMed - indexed for MEDLINE]

Appl Environ Microbiol 1992 Aug;58(8):2345-54

Molecular cloning of the Clostridium botulinum structural gene encoding the type B neurotoxin and determination of its entire nucleotide sequence.

Whelan SM, Elmore MJ, Bodsworth NJ, Brehm JK, Atkinson T, Minton NP.

Division of Biotechnology, PHLS Centre for Applied Microbiology and Research, Salisbury, Wiltshire, United Kingdom.

DNA fragments derived from the Clostridium botulinum type A neurotoxin (BoNT/A) gene (botA) were used in DNA-DNA hybridization reactions to derive a restriction map of the region of the C. botulinum type B strain Danish chromosome encoding botB. As the one probe encoded part of the BoNT/A heavy (H) chain and the other encoded part of the light (L) chain, the position and orientation of botB relative to this map were established. The temperature at which hybridization occurred indicated that a higher degree of DNA homology occurred between the two genes in the H-chain-encoding region. By using the derived restriction map data, a 2.1-kb BglII-XbaI fragment encoding the entire BoNT/B L chain and 108 amino acids of the H chain was cloned and characterized by nucleotide sequencing. A contiguous 1.8-kb XbaI fragment encoding a further 623 amino acids of the H chain was also cloned. The 3' end of the gene was obtained by cloning a 1.6-kb fragment amplified from genomic DNA by inverse polymerase chain reaction. Translation of the nucleotide sequence derived from all three clones demonstrated that BoNT/B was composed of 1,291 amino acids. Comparative alignment of its sequence with all currently characterized BoNTs (A, C, D, and E) and tetanus toxin (TeTx) showed that a wide variation in percent homology occurred dependent on which component of the dichain was compared. Thus, the L chain of BoNT/B exhibits the greatest degree of homology (50% identity) with the TeTx L chain, whereas its H chain is most homologous (48% identity) with the BoNT/A H chain. Overall, the six neurotoxins were shown to be composed of highly conserved amino acid domains interceded with amino acid tracts exhibiting little overall similarity. In total, 68 amino acids of an average of 442 are absolutely conserved between L chains and 110 of 845 amino acids are conserved between H chains. Conservation of Trp residues (one in the L chain and nine in the H chain) was particularly striking. The most divergent region corresponds to the extreme carboxy terminus of each toxin, which may reflect differences in specificity of binding to neurone acceptor sites.

J Biol Chem 1990 Jun 5;265(16):9153-8

The complete sequence of botulinum neurotoxin type A and comparison with other clostridial neurotoxins.

Binz T, Kurazono H, Wille M, Frevert J, Wernars K, Niemann H.

Institut fur Medizinische Virologie der Justus-Liebig-Universitat, Giessen, Federal Republic of Germany.

The seven serologically different botulinum neurotoxins are highly potent protein toxins that inhibit neurotransmitter release from peripheral cholinergic synapses. The activated toxins consist of the toxifying A-subunits (Mr approximately 50,000) linked by a disulfide bond to the receptor-binding BC-subunits (Mr approximately 100,000). We have established the complete sequence of botulinum neurotoxin type A (BoNT/A; 1,296 amino acid residues, Mr = 149,425) and a partial sequence of botulinum neurotoxin type E (273 amino acid residues) as deduced from the corresponding nucleotide sequences of the chromosomally located structural genes. The promoter of the BoNT/A gene is inactive in Escherichia coli. Primer extension experiments indicated that initiation of transcription of the BoNT/A gene occurred 118 nucleotides upstream from the ATG codon. A comparison of the protein sequence revealed an overall identity of 33.8% to that of tetanus toxin. No significant similarity to other known proteins including ADP-ribosylating toxins could be detected. Three of the six histidine residues of the A-subunit of BoNT/A were found in the peptide sequence H223ELIHXXH230 within a domain of predicted alpha-helical secondary structure. This motif is also found in similar positions of the A-subunits of tetanus toxin and BoNT/E.

PMID: 2160960 [PubMed - indexed for MEDLINE]

P10844. Botulinum neuroto...[gi:399134]

Links

LOCUS BXB_CLOBO 1291 aa linear BCT 15-JUN-2002
DEFINITION Botulinum neurotoxin type B precursor (BoNT/B) (Bontoxilysin B).
ACCESSION P10844
VERSION P10844 GI:399134
DBSOURCE swissprot: locus BXB_CLOBO, accession P10844;
class: standard.
extra accessions:P10843,created: Jul 1, 1989.
sequence updated: Jul 1, 1993.
annotation updated: Jun 15, 2002.
xrefs: gi: 144734, gi: 144735, gi: 40383, gi: 40384, gi: 407782,
gi: 407783, gi: 98574, gi: 80489, gi: 80488, gi: 98573, gi: 98572,
gi: 477374
xrefs (non-sequence databases): HSSPP10845, MEROPSM27.002,
InterProIPR000395, InterProIPR000130, PfamPF01742, PRINTSPR00760,
ProDomPD001963, PROSITEPS00142
KEYWORDS Neurotoxin; Transmembrane; Hydrolase; Metalloprotease; Zinc.
SOURCE Clostridium botulinum
ORGANISM Clostridium botulinum
Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae;
Clostridium.
REFERENCE 1 (residues 1 to 1291)
AUTHORS Whelan,S.M., Elmore,M.J., Bodsworth,N.J., Brehm,J.K., Atkinson,T.
and Minton,N.P.
TITLE Molecular cloning of the Clostridium botulinum structural gene
encoding the type B neurotoxin and determination of its entire
nucleotide sequence
JOURNAL Appl. Environ. Microbiol. 58 (8), 2345-2354 (1992)
MEDLINE 92384550
REMARK SEQUENCE FROM N.A.
REFERENCE 2 (residues 1 to 1291)
AUTHORS Szabo,E.A., Pemberton,J.M. and Desmarchelier,P.M.
TITLE Direct Submission
JOURNAL Submitted (~APR-1992)
REMARK SEQUENCE OF 35-245 FROM N.A.
STRAIN=NCTC 7273
REFERENCE 3 (residues 1 to 1291)
AUTHORS Campbell,K.D., Collins,M.D. and East,A.K.
TITLE Gene probes for identification of the botulinal neurotoxin gene and
specific identification of neurotoxin types B, E, and F
JOURNAL J. Clin. Microbiol. 31 (9), 2255-2262 (1993)

MEDLINE 94013372
REMARK SEQUENCE OF 633-993 FROM N.A.
STRAIN=NCTC 7273
REFERENCE 4 (residues 1 to 1291)
AUTHORS Dasgupta,B.R. and Datta,A.
TITLE Botulinum neurotoxin type B (strain 657): partial sequence and similarity with tetanus toxin
JOURNAL Biochimie 70 (6), 811-817 (1988)
MEDLINE 89000987
REMARK SEQUENCE OF 1-44 AND 441-466.
STRAIN=657
REFERENCE 5 (residues 1 to 1291)
AUTHORS Schmidt,J.J., Sathyamoorthy,V. and DasGupta,B.R.
TITLE Partial amino acid sequences of botulinum neurotoxins types B and E
JOURNAL Arch. Biochem. Biophys. 238 (2), 544-548 (1985)
MEDLINE 85197963
REMARK SEQUENCE OF 1-16 AND 441-458.
STRAIN=OKRA
REFERENCE 6 (residues 1 to 1291)
AUTHORS Schiavo,G., Rossetto,O., Santucci,A., DasGupta,B.R. and Montecucco,C.
TITLE Botulinum neurotoxins are zinc proteins
JOURNAL J. Biol. Chem. 267 (33), 23479-23483 (1992)
MEDLINE 93054694
REMARK IDENTIFICATION AS ZINC-PROTEASE.
REFERENCE 7 (residues 1 to 1291)
AUTHORS Schiavo,G., Benfenati,F., Poulain,B., Rossetto,O., Polverino de Laureto,P., DasGupta,B.R. and Montecucco,C.
TITLE Tetanus and botulinum-B neurotoxins block neurotransmitter release by proteolytic cleavage of synaptobrevin
JOURNAL Nature 359 (6398), 832-835 (1992)
MEDLINE 93063293
REMARK IDENTIFICATION OF SUBSTRATE.
COMMENT On or before Sep 14, 1993 this sequence version replaced gi:115189, gi:115190.

---.
[FUNCTION] BOTULINUS TOXIN ACTS BY INHIBITING NEUROTRANSMITTER RELEASE. IT BINDS TO PERIPHERAL NEURONAL SYNAPSES, IS INTERNALIZED

AND MOVES BY RETROGRADE TRANSPORT UP THE AXON INTO THE SPINAL
CORD
WHERE IT CAN MOVE BETWEEN POSTSYNAPTIC AND PRESYNAPTIC
NEURONS. IT
INHIBITS NEUROTRANSMITTER RELEASE BY ACTING AS A ZINC
ENDOPEPTIDASE
THAT CLEAVES THE 76-GLN-|-PHE-77 BOND OF SYNAPTOBREVIN-2.
[CATALYTIC ACTIVITY] Limited hydrolysis of proteins of the
neuroexocytosis apparatus, synaptobrevins, SNAP25 or syntaxin. No
detected action on small molecule substrates.
[COFACTOR] Binds 1 zinc ion per subunit (By similarity).
[SUBUNIT] DISULFIDE-LINKED HETERODIMER OF A LIGHT CHAIN (L) AND A
HEAVY CHAIN (H). THE LIGHT CHAIN HAS THE PHARMACOLOGICAL
ACTIVITY,
WHILE THE N-AND C-TERMINAL OF THE HEAVY CHAIN MEDIATE CHANNEL
FORMATION AND TOXIN BINDING, RESPECTIVELY.
[SUBCELLULAR LOCATION] Secreted.
[MISCELLANEOUS] THERE ARE SEVEN ANTIGENICALLY DISTINCT FORMS
OF
BOTULINUM NEUROTOXIN: TYPES A, B, C1, D, E, F, AND G.
[SIMILARITY] BELONGS TO PEPTIDASE FAMILY M27.

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     Protein         1..1291
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                     /note="BOTULINUM NEUROTOXIN B, LIGHT-CHAIN."
     Region          30
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                     /region_name="Conflict"
                     /note="T -> M (IN REF. 4)."
     Region          218
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                     /note="R -> G (IN REF. 2)."
     Region          225
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                /bond_type="disulfide"
                /note="INTERCHAIN (PROBABLE)."
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                /note="BOTULINUM NEUROTOXIN B, HEAVY-CHAIN."
     Region     464
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                /region_name="Conflict"
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ORIGIN
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       61 kssgifnrdv ceyydpdyln tndkkniflq tmiklfnrik skplgeklle miingipylg
      121 drrvpleefn tniasvtvnk lisnpgever kkgifanlii fgpgpvlnen etidigiqnh
      181 fasregfggi mqmkfcpeyv svfnnvqenk gasifnrrgy fsdpalilmh elihvlhgly
      241 gikvddlpiv pnekkffmqs tdaiqaeely tfggqdpsii tpstdksiyd kvlqnfrgiv
      301 drlnkvlvci sdpnininiy knkfkdkykf vedsegkysi dvesfdklyk slmfgftetn
      361 iaenykiktr asyfsdslpp vkiknlldne iytieegfni sdkdmekeyr gqnkainkqa
      421 yeeiskehla vykiqmcksv kapgicidvd nedlffiadk nsfsddlskn erieyntqsn
      481 yiendfpine lildtdlisk ielpsentes ltdfnvdvpv yekqpaikki ftdentifqy
      541 lysqtfpldi rdisltssfd dallfsnkvy sffsmdyikt ankvveaglf agwvkqivnd
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1201 sdefyntiqi keydeqptys cqllfkkdee stdeigligi hrfyesgivf eeykdyfcis
1261 kwylkevkrk pynlklgcnw qfipkdegwt e
//

Revised: July 5, 2002.

FEMS Microbiol Lett 1992 Feb 1;70(1):69-72

Related Articles, Links

Cloning of a Clostridium botulinum type B toxin gene fragment encoding the N-terminus of the heavy chain.

Jung HH, Rhee SD, Yang KH.

Department of Life Science, Korea Advanced Institute of Science and Technology, Taejon, Korea.

Two lambda gt11 clones of the toxin gene of Clostridium botulinum type B were identified by the monoclonal antibody specific to the heavy chain of type B toxin. Neither of the expressed fusion proteins from the lysates of lysogenic E. coli Y1089 showed any botulinal toxic activity. One of the clones hybridized to the oligonucleotide probe which was synthesized according to the amino acid sequence of N-terminus of heavy chain. The sequence analysis revealed that highly homologous regions in N-terminus of heavy chain exist among botulinum neurotoxins (type A, B) and tetanus toxin on the amino acid sequence level.

Ann Clin Lab Sci 1988 Jan-Feb;18(1):58-71

Related Articles, Links

Bacterial toxins.

Lubran MM.

Department of Pathology, Harbor-UCLA Medical Center, Torrance 90509.

Many bacterial toxins are proteins, encoded by the bacterial chromosomal genes, plasmids or phages. Lysogenic phages form part of the chromosome. The toxins are usually liberated from the organism by lysis, but some are shed with outer membrane proteins in outer membrane vesicles. An important non-protein toxin is lipopolysaccharide or endotoxin, which is a constituent of the cell wall of gram negative bacteria. Toxins may damage the eukaryotic cell membrane by combining with some structural component, or otherwise alter its function. Many toxins combine with specific receptors on the surface membrane, frequently glycoproteins or gangliosides, and penetrate the cell to reach their intracellular target. A common mechanism of entry is absorptive endocytosis. Many protein toxins have an A-B structure, B being a polypeptide which binds to the receptor and A being an enzyme. Many toxins are activated, either when produced by the bacterium or when bound to the membrane receptor, by proteases (nicking). An enzymatic process common to many toxins is adenosine diphosphate (ADP)-ribosylation of the adenylate cyclase regulatory proteins, leading to an increase in intracellular cyclic adenosine monophosphate (cAMP). This is the mechanism of action of cholera toxin. Diphtheria toxin catalyzes the transfer of ADP-ribose to elongation factor-2, inhibiting protein synthesis. Most toxins act on the target cells to which they bind, but tetanus toxin, and, to a lesser degree, botulinum toxin, ascend axons and affect more distant structures. Although many toxin effects caused by bacteria have been described, only a few toxins have been identified, characterized, and their mode of action determined at the molecular level. The best known of these are discussed.

Publication Types:
- Review
- Review, Tutorial

PMID: 3281562 [PubMed - indexed for MEDLINE]

Biochimie 1988, 70 (6):811-7

Related Articles by NCBI

Botulinum neurotoxin type B (strain 657): partial sequence and similarity with tetanus toxin.

Dasgupta,B R. , Datta,A.

Food Research Institute, University of Wisconsin, Madison 53706.

The type B neurotoxin (NT) isolated from Clostridium botulinum (strain 657) behaved as a mixture of single (unnicked) and dichain (nicked) proteins, both of Mr approximately 150 kDa. When the dichain NT was reduced by mercaptoethanol, the two chains migrated in sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) as separate polypeptides of Mr approximately 100 and 50 kDa that appeared similar to the heavy and light chains of other serotypes of botulinum NT. The N-terminal amino acid sequences of the two chains were determined. They were as follows: light chain:
Pro-Val-Thr-Ile-Asn-Asn-Phe-Asn-Tyr-Asn-Asp-Pro-Ile-Asp-Asn-Asn-Asn-Ile- Ile-Met -

Met-Glu-Pro-Pro-Phe-Ala-Arg-Gly-Met-Gly-Arg-Tyr-Tyr-Lys-Ala-Phe-Lys-Ile- Thr-Asp - Arg-Ile-Trp-Ile-; and heavy chain:

Ala-Pro-Gly-Ile-X-Ile-Asp-Val-Asp-Asn-Glu-Asp-Leu-Phe-Phe-Ile-Ala-Asp-Ly s-Asn-Ser-Phe-Arg-Asp-Asp-Leu-. These two sequences matched exactly with those of the light and heavy chains of type B NT (strain Okra) of which only 16 and 18 residues were known (J. Biol. Chem. (1985) 260, 10461). The above sequences were different from those of type A NT.

Immunoprecipitation reactions of type B NT isolated from strains 657 and Okra were indistinguishable against polyclonal anti-type B NT serum. These two preparations did not produce

precipitin reactions with polyclonal anti-type A NT serum.(ABSTRACT TRUNCATED AT 250 WORDS)

MedlineID: 89000987

PMID: 3139097

ISSN: 0300-9084

Eur J Biochem 1988 Nov 15;177(3):683-91

Related Articles, Links

Involvement of the constituent chains of botulinum neurotoxins A and B in the blockade of neurotransmitter release.

Maisey EA, Wadsworth JD, Poulain B, Shone CC, Melling J, Gibbs P, Tauc L, Dolly JO.

Department of Biochemistry, Imperial College, London, England.

1. The abilities of botulinum neurotoxins, types A and B (single and two-chain forms) to inactivate an intraneuronal component required for transmitter release were quantified in a phrenic-nerve-diaphragm preparation, cerebrocortical synaptosomes or the buccal ganglion of Aplysia californica and compared with the mouse toxicity assay. 2. Homogeneous preparations of the individually renatured polypeptide chains of both toxin types showed low residual toxicity in the whole animal and had no

effect on neurotransmission in all three systems, when tested singly. 3. Mixtures of individually renatured heavy chain, from type A or B, and either light chain proved very effective in blocking the evoked release of acetylcholine when bath-applied to the buccal ganglion of Aplysia whilst they were relatively inactive on mammalian nerve terminals, indicating a less efficient uptake of the polypeptides in the latter. 4. When renatured together, the homologous, but not the heterologous, chains of each toxin type yielded toxic, disulphide-linked two-chain species. 5. A role for the heavy chain alone in acceptor recognition and membrane translocation was implicated by the blockade of acetylcholine release produced when light chain was applied to a ganglion of Aplysia previously bathed in heavy chain and washed extensively. No blockade was observed when the order of application of the two chains was reversed. 6. These findings are discussed in the context of the intracellular requirement for both the constituent toxin chains for toxicity, and in the apparent need for these chains to be linked via a disulphide bond for uptake in rodents but not in Aplysia.

J Clin Microbiol 1993 Sep;31(9):2255-62

Related Articles, Links

Gene probes for identification of the botulinal neurotoxin gene and specific identification of neurotoxin types B, E, and F.

Campbell KD, Collins MD, East AK.

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A polymerase chain reaction method was developed for the specific detection of the botulinum neurotoxin (BoNT) gene of Clostridium botulinum. Degenerate oligonucleotide primers, designed from the nucleotide sequence of the heavy chain of the BoNT gene, amplified a specific fragment of approximately 1.1 kb from strains of C. botulinum toxin types A, B, E, F, and G and neurotoxin-producing strains of Clostridium barati and Clostridium butyricum, but no fragment was obtained from nontoxigenic strains. The fragments amplified from several strains of C. botulinum types B, E, and F were cloned in Escherichia coli and their nucleotide sequences were determined. Sequences within this region were used to design oligonucleotide probes specific for BoNT type B (BoNT/B), BoNT/E, and BoNT/F genes. An additional probe was designed for the detection of the BoNT/F gene of C. barati, which differed in sequence from BoNT/F genes of both proteolytic and nonproteolytic strains of C. botulinum.

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